

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

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Applicant's or agent's file reference 920214.00005	FOR FURTHER ACTION		See Form PCT/IPEA/416																								
International application No. PCT/US04/05340	International filing date (day/month/year) 24 February 2004 (24.02.2004)	Priority date (day/month/year) 25 February 2003 (25.02.2003)																									
International Patent Classification (IPC) or national classification and IPC IPC(7): C07H 5/06; C07K 7/00, 9/00 and US Cl.: 514/8, 17, 23, 25, 53; 530/322; 536/55.2, 55.3																											
Applicant THE ARIZONA BOARD OF REGENTS ON BEHALF OF THE UNIVERSITY OF ARIZONA																											
<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of <u>6</u> sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p style="margin-left: 20px;">a. <input type="checkbox"/> (sent to the applicant and to the International Bureau) a total of ___ sheets, as follows:</p> <p style="margin-left: 40px;"><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p style="margin-left: 40px;"><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p style="margin-left: 20px;">b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p> <p>4. This report contains indications relating to the following items:</p> <table style="width: 100%; border: none;"> <tr> <td style="width: 10%;"><input checked="" type="checkbox"/></td> <td style="width: 20%;">Box No. I</td> <td>Basis of the report</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. II</td> <td>Priority</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. III</td> <td>Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. IV</td> <td>Lack of unity of invention</td> </tr> <tr> <td><input checked="" type="checkbox"/></td> <td>Box No. V</td> <td>Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. VI</td> <td>Certain documents cited</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. VII</td> <td>Certain defects in the international application</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. VIII</td> <td>Certain observations on the international application</td> </tr> </table>				<input checked="" type="checkbox"/>	Box No. I	Basis of the report	<input type="checkbox"/>	Box No. II	Priority	<input type="checkbox"/>	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability	<input type="checkbox"/>	Box No. IV	Lack of unity of invention	<input checked="" type="checkbox"/>	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement	<input type="checkbox"/>	Box No. VI	Certain documents cited	<input type="checkbox"/>	Box No. VII	Certain defects in the international application	<input type="checkbox"/>	Box No. VIII	Certain observations on the international application
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Date of submission of the demand 24 February 2004 (24.02.2004)	Date of completion of this report 27 April 2005 (27.04.2005)																										
Name and mailing address of the IPEA/ US Mail Stop PCT, Attn: IPEA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Authorized officer <i>Portia Lawrence for</i> Bennett Celsa Telephone No. 571.272.1600																										

Form PCT/IPEA/409 (cover sheet)(January 2004)

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/US04/05340

Box No. I Basis of the report

1. With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ This report is based on translations from the original language into the following language _____, which is the language of a translation furnished for the purposes of:
- ☐ international search (under Rules 12.3 and 23.1(b))
- ☐ publication of the international application (under Rule 12.4)
- ☐ international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the elements of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:
- ☒ the international application as originally filed/furnished
- ☒ the description:
pages 1-10 as originally filed/furnished
pages* NONE received by this Authority on _____
pages* NONE received by this Authority on _____
- ☒ the claims:
pages 11 and 12 as originally filed/furnished
pages* NONE as amended (together with any statement) under Article 19
pages* NONE received by this Authority on _____
pages* NONE received by this Authority on _____
- ☒ the drawings:
pages 1-4 as originally filed/furnished
pages* NONE received by this Authority on _____
pages* NONE received by this Authority on _____
- ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing
3. ☒ The amendments have resulted in the cancellation of:
- ☒ the description, pages NONE
- ☒ the claims, Nos. NONE
- ☒ the drawings, sheets/figs NONE
- ☒ the sequence listing (*specify*): NONE
- ☒ any table(s) related to the sequence listing (*specify*): NONE
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
- ☐ the description, pages _____
- ☐ the claims, Nos. _____
- ☐ the drawings, sheets/figs _____
- ☐ the sequence listing (*specify*): _____
- ☐ any table(s) related to the sequence listing (*specify*): _____

* If item 4 applies, some or all of those sheets may be marked "superseded."

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/US04/05340**Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement****1. Statement**

Novelty (N)

Claims 3,8 and 9 YESClaims 1,2,4-7 and 10 NO

Inventive Step (IS)

Claims NONE YESClaims 1-10 NO

Industrial Applicability (IA)

Claims 1-10 YESClaims NONE NO**2. Citations and Explanations (Rule 70.7)**

Please See Continuation Sheet

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of:

Claims 1 and 4-7 lacks novelty under PCT Article 33(2) as being anticipated by HORVAT, S et al.

Horvat et al. disclose analgesic enkephalin derivatives (e.g. with morphine-like action i.e. analgesia) comprising the disaccharide modified peptides comprising the motif YGGF (e.g. see compounds 8a-8f) in which the making of pharmaceuticals with delivery vehicles (e.g. packages/instruction) for human use would be immediately envisaged to one of ordinary skill in the art in view of the known use of enkephalin derivatives as analgesics. Additionally, the properties (e.g. ability to cross blood-brain barrier) is inherent in the reference peptides.

Claims 1 and 4-7 lack novelty under PCT Article 33(2) as being anticipated by MITCHELL et al.

Mitchell et al. disclose analgesic enkephalin derivatives comprising disaccharide modified peptides comprising the motif YxGF (where x is a D-amino acid: see e.g. compounds 14-16 comprising lactose, cellobiose and mellibiose, respectively) in which the making of pharmaceuticals with delivery vehicles (e.g. packages/instruction) for human use would be immediately envisaged to one of ordinary skill in the art in view of the known use of enkephalin derivatives as analgesics. Additionally, the properties (e.g. ability to cross blood-brain barrier) is inherent in the reference peptides.

Claims 1, 4-5 and 7 lack novelty under PCT Article 33(2) as being anticipated by FASEB JOURNAL (March 8, 2001) Abstract ("Antinociceptive Structure Activity Studies With Novel Opioid Glycopeptides").

The Abstract teaches that disaccharide modification of enkephalin-based opioid peptides optimally provides (e.g. versus mono/tri saccharide modification) CNS bioavailability (via blood brain barrier) in which the making of pharmaceuticals with delivery vehicles (e.g. packages/instruction) for human use would be immediately envisaged to one of ordinary skill in the art in view of the known use of enkephalin derivatives as analgesics

Claims 1-2, 4-7 and 10 lack novelty under PCT Article 33(2) as being anticipated by PALIAN et al. or POLT et al. Abstract.

Both the PALIAN et al. article and the POLT Abstract teach the ability of enkephalin derivatives comprising disaccharide (E.g. b-maltose) YtGF motif to cross the blood brain barrier in which the making of pharmaceuticals with delivery vehicles (e.g. packages/instruction) for human use would be immediately envisaged to one of ordinary skill in the art in view of the known use of enkephalin derivatives as analgesics. These "P" references are being citable against the presently claimed invention since the 60449989

Supplemental Box

priority document fails to provide support (e.g. only discloses one disaccharide species) for the breadth (E.g. genus) of the presently claimed invention.

Claims 1-10 lack an inventive step under PCT Article 33(3) as being obvious over U.S. Pat. No. 4,407,794 in view of MITCHELL et al. and FASEB JOURNAL Abstract.

The '794 patent disclose enkephalin compounds comprising YxGF (x is a D-amino acid including dThr) which differs from the presently claimed invention by failing to teach modification with an O-linked serine disaccharide (e.g. lactose, mellibiose or maltose).

However, modification of enkephalin compounds thru O-linked serines to disaccharides (e.g. lactose/mellibiose/maltose) in order to increase absorption by increasing blood-brain barrier transport is taught by the MITCHELL and FASEB JOURNAL references.

Accordingly, it would have been obvious to modify the '794 patent compounds with an O-linked serine disaccharide (e.g. lactose, mellibiose or maltose) and arrive at the presently claimed compounds in order to obtain improved blood-brain barrier transport.

Claims 1-10 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.